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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,187	07/09/2003	Ann M. Lees	10797-004005	5109

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EXAMINER	
RINAUDO, JO ANN S	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,187	LEES ET AL.	
	Examiner	Art Unit	
	Jo Ann Rinaudo	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *66-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,10,12-19,23,29,30,34-38,44-48,54,56,58,59,62 and 63* is/are rejected.

7)☒ Claim(s) *6-8, 11, 20-22, 24-28, 31-33, 39-43, 49-53, 55, 57, 60, 61, 64, and 65* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-71 are pending.

2. Applicant's election with traverse of Group II (Claims 1-6, 12-20, 29-31, 34-38, 44-48, 54, 56, 58, 59, 62, and 63) in a reply filed on 08 September 2005 is acknowledged. The traversal is on the grounds that because of the relatedness of the human LBP-2 sequences of SEQ ID NO:43 (Group II) and SEQ ID NO:7 (Group IV), the issues raised during the examination of antibodies raised against the sequences are expected to be similar. SEQ ID NO: 43 encompasses SEQ ID NO: 7. Upon consideration of the Applicant's arguments, filed on 08 September 2005, the restriction between Group II and Group IV is hereby withdrawn. The prior art search has been extended to include SEQ ID NO:7.

3. The requirement for restriction between newly combined Group II and IV and Groups I, III, and V-VIII is still deemed proper and is therefore made FINAL.

4. Claims 66-71 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

5. Claims 1-65 are under consideration as they are drawn to a humanized, chimeric, or human antibody or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) polypeptide of SEQ ID NO: 7 or SEQ ID NO: 43, wherein the antibody or fragment thereof blocks binding of LDL to the LBP-2 polypeptide, and wherein the antibody or fragment thereof comprises a label; a pharmaceutical composition comprising the antibody or fragment thereof; and hybridoma cell lines producing the antibody.

6. Applicant's IDS filed on 13 February 2004 is acknowledged and has been considered. However, IDS Reference No. AV is directed to GenBank Accession No.

NM005717 and searching for this Reference in GenBank produced an error message. Therefore, IDS Reference No. AV has been lined through and was not considered.

7. Claims 18 and 29 are objected to because they contain typographical errors. Claim 18 contains the terms "antibody or antibody or" and Claim 29 contains the terms "that that". Correction of errors is required.

8. The following is a quotation from 35 U.S.C. §101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1-3, 5-9, and 11 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

10. Claims 1-3, 5-9, and 11, as written, does not sufficiently distinguish over antibodies as they exist naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated". See MPEP 2105.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 4 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 4 and 10 are indefinite in the recitation of "comprising an antibody that is a monoclonal antibody". The term "comprising" is open-ended and expands the antibody to include an additional non-disclosed antibody. It is suggested that "comprising an antibody" be amended to recite "wherein the antibody is a monoclonal antibody."

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

15. Claims 1-5, 9, 12-19, 23, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated monoclonal, polyclonal, humanized, chimeric, or human antibody, or fragment thereof, that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) polypeptide of SEQ ID NO: 7 or SEQ ID NO: 43; wherein said antibody fragment comprises an Fab, Fab', $F(ab')_2$, or F(v) fragment; and a pharmaceutical composition comprising an antibody of SEQ ID NO: 7 or SEQ ID NO: 43, or fragment thereof; and a hybridoma cell line that produces the antibody of SEQ ID NO: 7 or SEQ ID NO: 43, *does not reasonably provide enablement for* a monoclonal, polyclonal, humanized, chimeric, or human antibody, or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) (Claims 1-4, 12-18, 29 and 30); wherein the antibody fragment comprises a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain (Claims 3 and 14); an antibody fragment that specifically binds to SEQ ID NO: 7 comprising a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain (Claims 9 and 23); an antibody or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) blocks binding of

low density lipoprotein to the LBP-2 polypeptide (Claims 5 and 19); antibody or fragment thereof specifically binds to a low density lipoprotein binding protein-2 (LBP-2) comprises a radiolabel, a technetium-binding ligand, or a gadolinium-binding chelator, wherein the gadolinium-binding chelator is diethylene triamine penta-acetic acid (DTPA) (Claims 34-38, 44-48); a pharmaceutical composition comprising an antibody or fragment thereof specifically binds to a low density lipoprotein binding protein-2 (LBP-2) (Claims 54 and 56); and hybridoma cell lines producing antibodies and fragments thereof that specifically bind to a low density lipoprotein binding protein-2 (LBP-2) (Claims 58, 59, 62 and 63). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

16. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, and the amount of experimentation required to enable one skilled in the art to practice the invention.

17. The scope of the claimed antibody, an antibody that specifically binds to a low density lipoprotein binding protein-2 (LBP-2), or fragment thereof (Claims 1-4, 12-18, 29 and 30); an antibody or fragment thereof specifically binds to a low density lipoprotein binding protein-2 (LBP-2) comprises a radiolabel, a technetium-binding ligand, or a gadolinium-binding chelator, wherein the gadolinium-binding chelator is diethylene triamine penta-acetic acid (DTPA) (Claims 34-38, 44-48); a pharmaceutical composition comprising an antibody or fragment thereof specifically binds to a low density lipoprotein binding protein-2 (LBP-2) (Claims 54 and 56); and hybridoma cell lines producing antibodies and fragments thereof that specifically bind to a low density lipoprotein binding protein-2 (LBP-2) (Claims 58, 59, 62 and 63) is not commensurate with the enablement provided in the specification. Other than SEQ ID NO: 7 and SEQ ID

NO:43, the specification fails to provide guidance as to what other low density lipoprotein binding protein-2 (LBP-2) polypeptide sequences can be used to make an antibody that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) polypeptide. The amino acid sequence of a protein determines its structural and functional properties. These properties are important for antigenicity and therefore important for antibody specificity. For example, Bendayan (J. Histochem. Cytochem. 1995; 43: 881-886) characterizes the specific reactivity of a monoclonal antibody produced to human proinsulin, and shows that although the antibody is highly specific, it is nevertheless able to bind to not only human proinsulin, but to proinsulin from other species and even a distinct protein, glucagons, based upon conservation of an Arg-Arg dipeptide sequence in each of these molecules (see entire document). Bendayan concludes that "an antibody directed against such a sequence, although still yielding specific labeling, could reveal different molecules not related to the original antigen" (page 886, last paragraph). Therefore, there does not appear to be sufficient guidance in the specification as to how a skilled artisan would make the antibodies that specifically bind to a low density lipoprotein binding protein-2 (LBP-2), other than SEQ ID NO: 7 and 43, as recited in the instant claims.

18. The specification fails to provide guidance on how to make and use antibody fragments consisting of a "heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain" (Claims 3, 9, 14, and 23). The specification only discloses that antibody fragments include "heavy chain monomers, heavy chain dimers, heavy chain trimers, light chain monomers, light chain dimers, light chain trimers, dimers consisting of one heavy and one light chain" (page 24, lines 11-15, in particular). Hollinger et al. teach that single chain variable domain antibodies rarely retain the affinity of the parent antibody and are also poorly soluble and often prone to aggregation (see page 1127, columns 1 and 2 , Fab, Fv and single V-type domains; and page 1128, columns 1 and 2, and Figure 2, in particular). Furthermore, Hollinger et al. teach that to form dimers and trimers, the length of the linker region is important and

that the length of linkers affects stability (see page 1130, column 1, paragraph 1, in particular). Therefore, the lack of guidance, lack of sufficient working examples, and the amount of experimentation required does not enable one skilled in the art to make and use antibody fragments consisting of a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain that specifically bind to a low density lipoprotein binding protein-2 (LBP-2), as recited in the instant claims.

19. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

20. Claims 1-5, 9, 12-19, 23, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

21. Applicant is in possession of an isolated monoclonal, polyclonal, humanized, chimeric, or human antibody, or fragment thereof, that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) polypeptide of SEQ ID NO: 7 or SEQ ID NO: 43; wherein said antibody fragment comprises an Fab, Fab', $F(ab')_2$, or F(v) fragment; and a pharmaceutical composition comprising an antibody of SEQ ID NO: 7 or SEQ ID NO: 43, or fragment thereof; and a hybridoma cell line that produces the antibody of SEQ ID NO: 7 or SEQ ID NO: 43. The Applicant is not in possession of a monoclonal, polyclonal, humanized, chimeric, or human antibody, or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) (Claims 1-4, 12-18, 29 and 30); wherein the antibody fragment comprises a heavy chain monomer, a

heavy chain dimer, a heavy chain trimer, a light chain chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain (Claims 3 and 14); an antibody fragment that specifically binds to SEQ ID NO: 7 comprising a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain (Claims 9 and 23); an antibody or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) blocks binding of low density lipoprotein to the LBP-2 polypeptide (Claims 5 and 19); antibody or fragment thereof specifically binds to a low density lipoprotein binding protein-2 (LBP-2) comprises a radiolabel, a technetium-binding ligand, or a gadolinium-binding chelator, wherein the gadolinium-binding chelator is diethylene triamine penta-acetic acid (DTPA) (Claims 34-38, 44-48); a pharmaceutical composition comprising an antibody or fragment thereof specifically binds to a low density lipoprotein binding protein-2 (LBP-2) (Claims 54 and 56); and hybridoma cell lines producing antibodies and fragments thereof that specifically bind to a low density lipoprotein binding protein-2 (LBP-2) (Claims 58, 59, 62 and 63).

22. There is insufficient written description of an "antibody, or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) polypeptide" (Claims 1-5, 9, 12-19, 23, 29, 30, 34-38, 44-48, 54, 56, 58, 59, 62, and 63). There is insufficient possession of the "antibody, or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2)" that would be necessary to establish the relevant structural and functional characteristics. Applicant has only disclosed an antibody or fragment thereof that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) of SEQ ID NO: 7 or SEQ ID NO: 43; therefore, the skilled artisan cannot envision all the contemplated antibody possibilities recited in the instant claims.

23. In the specification, there is insufficient written description of an antibody fragment that specifically binds to low density lipoprotein binding protein-2 (LBP-2) polypeptide comprising "a heavy chain monomer, a heavy chain dimer, a heavy chain

trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain" (Claims 3, 9, 14, and 23) There is insufficient possession of the a heavy chain monomer, a heavy chain dimer, a heavy chain trimer, a light chain monomer, a light chain dimer, a light chain trimer, and a dimer consisting of one heavy and one light chain" necessary to establish the relevant structural and functional characteristics. Applicant has only disclosed an antibody or fragment thereof, comprising an Fab, Fab', $F(ab)_2$, or F(v) fragments, that specifically binds to a low density lipoprotein binding protein-2 (LBP-2) of SEQ ID NO: 7 or SEQ ID NO: 43; therefore, the skilled artisan cannot envision all the contemplated antibody possibilities recited in the instant claims.

24. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

25. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

26. Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

27. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

28. Claims 6-8, 11, 20-22, 24-28, 31-33, 39-43, 49-53, 55, 57, 60, 61, 64 and 65 are objected to as being dependent upon a rejected base claim and non-elected embodiments, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jo Ann Rinaudo whose telephone number is 571.272.8143. The examiner can normally be reached on M-F, 8:30AM - 5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571.272.0841. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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10/25/2005

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